201-16236

Isophthalonitrile

CAS # 626-17-5

HPV Test Plan: Revision Based on USEPA Comments

Syngenta Crop Protection, Inc.

April 2006

Summary

Syngenta Crop Protection, Inc (Syngenta) has agreed to participate in the United States Environmental Protection Agency's (EPA) voluntary High Production Volume (HPV) Chemical Program. The objective of EPA's HPV program is to provide basic hazard information for chemicals manufactured at high volumes in the United States. Syngenta hereby submits the test plan for isophthalonitrile (CAS# 626-l 7-5), which is used as an intermediate in the production of certain agricultural chemicals (e.g., fungicides).

IUPAC Name: Isophthalonitrile; Common Name: 1,3-dicarbonitrile benzene; Abbreviation: IPN; CAS#: 626-l 7-5

In 2005, Syngenta provided the test plan and an updated IUCLID document for isophthalonitrile (CAS# 626-17-5) under the High Production Volume (HPV) Chemical Challenge Program. The test plan identified existing data of adequate quality for isophthalonitrile, and outlined any intended testing to be conducted. On February 08, 2006, EPA commended Syngenta for its commitment to the HPV Challenge Program and provided comments on the isophthalonitrile HPV submission. Based on the EPA review of the isophthalonitrile test plans and robust summaries, EPA requested additional clarification and information on the following:

- **Physicochemical Properties.** The submitter needs to indicate whether certain of these endpoints are measured or estimated. If estimated, the submitter needs to provide measured data.
- **Environmental Fate.** The submitter needs to provide estimated or measured data for the photodegradation endpoint and measured data for the stability in water and biodegradation endpoints. For fugacity modeling, appropriate measured input values are needed.
- **Health Effects.** EPA reserves judgment on the adequacy of data for the gene mutations and developmental toxicity endpoints. The submitter needs to address deficiencies in the robust summaries.
- **Ecological Effects.** Adequate data are available for toxicity to fish for the purposes of the HPV Challenge Program. The submitter needs to provide adequate data for the invertebrates and algal toxicity endpoints and address deficiencies in the robust summaries.

This document addresses the agencies conclusions and provides additional information and testing plans to meet the EPA guidance. Furthermore, Syngenta agrees with the Physicians Committee for Responsible Medicine comments regarding isophthalonitrile that no additional mammalian toxicity is needed based on the quantity, quality and type of database that currently exist for this chemical. However, Syngenta does not agree with the Environmental Defense conclusion or logic regarding isophthalonitrile. Nevertheless, Syngenta will provide additional information regarding possible occupational and environmental exposure potential.

Syngenta Response to EPA Comments on the Isophthalonitrile HPV Challenge Program Submission

1) Physicochemical Properties

EPA Comment: "Adequate data are available for melting point and partition coefficient for the purposes of the HPV Challenge Program. The submitter provided limited information from MSDSs in the robust summaries for boiling point, vapor pressure, and water solubility. The submitter needs to verify that these data are measured or else provide measured data to address these endpoints. Estimated data are not adequate for the purposes of the HPV Challenge Program because the use of estimated values introduces uncertainties that become magnified in modeling applications. Data from published sources are acceptable, as long as the submitter identifies the source(s)."

Syngenta Response: Syngenta agrees that melting point and partition coefficient information are sufficient. The boiling point value of isophthalonitrile should be considered the same as the melting point because isophthalonitrile sublimes. The vapor pressure value of isophthalonitrile was obtained from estimates in published literature. However a measured/calculated value has been located/conducted. While this study is non-GLP and not published, the measured/calculated value is similar to the estimates. Similarly, the water solubility value of isophthalonitrile was obtained from estimates in published literature. However, a measured/calculated value has been located/conducted. While this study is non-GLP and not published, the measured/calculated values is an order of magnitude less than the estimates. Where there were differences between the estimated and measured values in vapor pressure and water solubility, the more conservative values were used in the Epiwin runs.

Data inputs to Epiwin v. 3.11 estimation program (in bold):

Parameter	Input	Type	Source
Henry's Law constant	**5.03 x 10^{-7} atm-m^3/mol** at 25°C (Syngenta calc'd value = 9.31 x 10^{-7} atm-m^3/mol)	Estimated	Meylan & Howard (1991)" (Unpublished Syngenta study)
Water solubility	**1.05 x 10^4 mg/L** at 25°C (Syngenta calc'd value = 900 mg/L)	Estimated	Meylan, *et al.* (1996)* (Unpublished Syngenta study)
Vapor pressure	**0.00569 mm Hg** at 25°C (Syngenta VPC value = 0.00497 mm Hg at 25°C)	Estimated	Neely & Blau (1985)* (Unpublished Syngenta study)
Melting point	**162°C**	-	CRC handbook, 63rd Ed.
Boiling point	Sublimes	-	*Chem. Ber.* **9** 1478, 1483 (1875)
Log K_{ow}	**0.80**	Experimental	Hansch, *et al.* (1995)*

*Syracuse Research Corporation, http://chem.sis.nlm.nih.gov/chemidplus/

2) Environmental Fate

EPA Comment: "The submitters proposal to provide only modeling data for all endpoints (as indicated on page 3 of the test plan) is not adequate for the purposes of the HPV Challenge Program.

Photodegradation. Estimated or measured photodegradation data are adequate for the purposes of the HPV Challenge Program.

Stability *in* water. The submitter needs to provide measured stability in water (hydrolysis) data following OECD Guideline 111.

Biodegradation. The submitter needs to provide measured ready biodegradation data following OECD Guideline 301.

Fugacity. EPA agrees that Level III modeling data will address the fugacity endpoint. However, the submitter needs to input appropriate measured values to develop these data. The use of estimated values introduces uncertainties that then become magnified in modeling applications."

Syngenta Response: Based on recent communications with EPA, the EPA indicated that the estimated photodegradation data with isophthalonitrile will be sufficient to meet the HPV requirement based on the existence of the other measured and estimated physiochemical information and the Epiwin Suite (AOP program) output.

As far as Syngenta is aware, no hydrolysis data are available for isophalonitrile. Based on discussions with the EPA, Syngenta proposes to conduct a limited test for hydrolysis (e.g., hydrolysis at 50C at pH 5, 7, and 9). However, there is unlikely to be significant hydrolysis under these relatively mild conditions, so Syngenta requests the opportunity to accept that the product is "stable" under hydrolysis conditions and use this conservative approach when addressing exposure potential.

Syngenta is unaware of any biodegradation data for isophthalonitrile. In discussions with the EPA, Syngenta has identified a limited test for ready biodegradation by activated sludge that will be sufficient to meet regulatory needs. Syngenta proposes to conduct a biodegradation study because no other data could logically be bridged to satisfy the microbial degradation characteristics of isophthalonitrile.

As requested, the full Level III fugacity modeling output, using the data inputs in the table above, is appended to this response (Appendix 1).

3) Health Effects

EPA Comment: The submitted data for acute, repeated-dose, chromosomal and reproductive toxicity are adequate for the purposes of the HPV Challenge Program. EPA reserves judgement on the adequacy of data for the gene mutation and developmental toxicity endpoints pending the submission of additional information.

Genetic Toxicity (gene mutations). The submitter needs to provide the response of the positive controls to validate the negative results of the assay.

Developmental toxicity. No robust summary data were submitted for this endpoint. The submitter concludes from the combination 28-day repeated-dose toxicity and one-generation rat reproduction study that there was no obvious/gross teratogenicity. The submitter needs to provide a separate robust summary for the developmental toxicity endpoint highlighting pertinent study parameters, with the following additional information: gross abnormalities, sexes of the litter, litter size, litter weights, post-natal growth of offspring, number of implantations, number of corpora lutea. EPA encourages the submission of an adequate study on an appropriate analog, if available, to strengthen the analysis for this endpoint.

Syngenta Response: *Genotoxicity*. In the genetic toxicity study (Ames Assay, study number CTL/C/3277), positive controls were conducted utilizing a number of positive controls [2-(2-furyl)-3-(5-nitro-2-furyl)acrylamide (TA100,WP2, TA98), sodium azide (TA1 535) and 9-aminoacridine (TA1537), 2-aminoanthracene (five strains)] with and without activation (S9 microsomal fractions). The robust summary will be updated with more details on the results from the positive control study (Appendix 2).

Developmental Toxicity Endpoints: Syngenta submitted an isophthalonitrile one-generation reproduction study in the rat (Syngenta study number 3795-91-0129-TX-003). In this study, gross abnormalities, sexes of the litter, litter size, litter weights, post-natal growth of offspring were measured as potential adverse effects. The number of implantations and corpora *lutea* were not directly measured in the study, however the endpoints were indirectly measured based on the reproductive outcome data from the study. Based on the results from the one-generation reproductive toxicity study in rats, the developmental toxicity hazard potential has been adequately addressed. Syngenta will provide a separate robust summary to emphasize the developmental toxicity endpoints and will submit this study to the EPA in support of the HPV Challenge Program.

In the study, rats were fed diet containing 0, 5, 10, 25, and 50 mg isophthalonitrile/kg/day for at least 122 days. Rats were mated for a total of 14 days. The date of delivery; the number, weight and sex of live and stillborn pups; and any external abnormalities were recorded. The weight, sex and number of live pups were recorded at regular intervals during lactation. Litters were culled to eight pups on day 4 of lactation. On Day 21 of lactation, 10 pups of each sex were selected with complete necropsy, and the above listed tissues [long list] were collected and saved for possible histopathological examination. The remaining pups were subjected to gross necropsies; any gross lesion were recorded and saved, and the carcasses were discarded. (Syngenta study number 3795-91-0129-TX-003, page 6-8)

In the reproductive phase, parental reproductive parameters appeared to be unaffected by isophthalonitrile administration. Effects of parental body weight and body weight gain similar to those seen during the 28-day feeding phase were noted during the reproductive phase of the study at 25 and 50 mg/kg/day. Apparent compound-related reproductive effects on offspring survival in *utero* were noted. This was evidenced by an increase in the number of stillborn pups with a corresponding decrease in the number of live born pups and litter size at 50 mg/kg/day, suggesting that isophthalonitrile is fetotoxic at this dietary concentration,

further suggesting that 25 mg/kg/day is the NOEL for reproductive results. (Syngenta study number 3795-91-0129-TX-003, page 9).

No compound-related effects on mating and fertility indices or gestation were noted. No compound-related effects on sex ratio were observed; the ratio of males to the total number of pups/litter was comparable between control and test groups. Pup bodyweights for all dose groups were 6 to 9 percent lower than controls pups on Day 0 of lactations; statistical differences were obtained at 5 and 50 mg/kg/day. These slight changes continued to Day 21 of lactation, but no statistically significant differences were noted. However, reductions were less than 10 percent of the control values at all intervals, and the lower body weight observed in high-dose pups was not considered to be biologically significant or compound related. Although, the small sample size precluded a definitive assessment of effects on the body weight of offspring.

No compound-related necropsy findings were observed in pups that were stillborn, died spontaneously, or were terminated (culled or 12-day old pups) during the study. The only findings observed at necropsy were yellow coloration, dilated renal pelvis (es), and distended cecum. The observations occurred with equal frequency in all groups, and no dose-related pattern was evident. No other abnormalities were noted.

4) Ecological Effects (fish, invertebrates, and algae)

EPA Comment: The submitted data for fish toxicity are adequate for the purposes of the HPV Challenge Program. No data were submitted for the invertebrate toxicity endpoint and the algal toxicity robust summary has a reliability code of 4 (unassignable). The submitter needs to provide adequate measured data for the invertebrate and algae toxicity endpoints.

Syngenta Response: Syngenta proposes to conduct an algal toxicity and daphnia EC50 study. Once the data is available, the robust summaries will be provided.

5) Occupational and Environmental Exposure potential with Isophthalonitrile

Isophthalonitrile is manufactured in a closed production system, transferred into bags (packaged), and the bagged material is manually added to the fungicide production system. Isophthalonitrile is completely reacted on-site to produce the final product. No residues of IPN remain in the finished fungicide.

Less than twenty-five workers are potentially exposed to isophthalonitrile during its production, bagging, and addition to the fungicide production equipment. Local exhaust ventilation equipment is used to control dust at the two manual handling locations to minimize occupational and environmental exposure. Workers wear protective clothing, gloves and respiratory protection to minimize their exposure to isophthalonitrile.

Industrial hygiene monitoring indicates that airborne isophthalonitrile levels in the packaging room (high potential exposure area) are well below current occupational exposure limits for IPN set by ACGIH and NIOSH.

IPN production presents no transportation issues, as it is totally consumed on site.

Appendix 1: Epiwin v. 3.11 Model Inputs and Results (including Level III Fugacity Model)

SMILES : C(#N)c(ccccIC(#N))cl

CHEM : 1,3-Benzenedicarbonitrile

CAS NUM: 000626-17-5

MOL FOR: C8 H4 N2

MOL WT: 128.13

----------EFSUMMARY _____

Physical Property Inputs:

Water Solubility (mg/L): 10500

Vapor Pressure (mm Hg) : 0.00569

Henry LC (atm-m3/mole) : 5.03E-007

Log Kow (octanol-water): 0.80

Boiling Point (deg C) : m-m---

Melting Point (deg C) : 162.00

KOWWIN Program (v1 .67) Results:

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Log Kow(version 1.67 estimate): 1.09

Experimental Database Structure Match:

Name : 1,3-Benzenedicarbonitrile

CAS Num : 000626-17-5

Exp Log P: 0.80

Exp Ref : Hansch,C et al. (1995)

SMILES : C(#N)c(cccc1 C(#N))c1

CHEM : 1,3-Benzenedicarbonitrile

MOL FOR: C8 H4 N2

MOL WT : 128.13

TYPE	NUM	LOGKOW FRAGMENT DESCRIPTION	COEFF	VALUE
Frag	6	Aromatic Carbon	0.2940	1.7640
Frag	2	-C#N [cyano, aromatic attach]	(-0.4530	-0.9060
Const		Equation Constant		0.2290

Log Kow = 1.0870

MPBPWIN (v1 .41) Program Results:

Experimental Database Structure Match:

Name : 1,3-DICYANOBENZENE

CAS Num : 000626-17-5

Exp MP (deg C): 162

Exp BP (deg C): ---

Exp VP (mm Hg): ---

SMILES : C(#N)c(ccccIC(#N))cl

CHEM : 1,3-Benzenedicarbonitrile

MOL FOR: C8 H4 N2

MOL WT : 128.13

SUMMARY MPBPWIN v1 .41

Boiling Point: 265.92 deg C (Adapted Stein and Brown Method)

Melting Point: 75.68 deg C (Adapted Joback Method)

Melting Point: 41.61 deg C (Gold and Ogle Method)

Mean Melt Pt : 58.64 deg C (Joback; Gold,Ogle Methods)

Selected MP: 58.64 deg C (Mean Value)

Vapor Pressure Estimations (25 deg C):

(Using BP: 265.92 deg C (estimated))

(Using MP: 162.00 deg C (user entered))

VP: 0.000446 mm Hg (Antoine Method)

VP: 0.000458 mm Hg (Modified Grain Method)

VP: 0.000929 mm Hg (Mackay Method)

Selected VP: 0.000458 mm Hg (Modified Grain Method)

TYPE	NUM	BOIL DESCRIPTION.	COEFF	VALUE
Group	4	CH (aromatic)	28.53	114.12
Group	2	-C (aromatic)	30.76	61.52
Group	2	-CN (to aromat)	95.43	190.86
*		Equation Constant		198.18
RESULT-uncorr		BOILING POINT in deg Kelvin		564.68
RESULT- corr		BOILING POINT in deg Kelvin		539.08
		BOILING POINT in deg C		265.92

TYPE	NUM	MELT DESCRIPTION	COEFF	VALUE
Group	4	CH (aromatic)	8.13	32.52
Group	2	-C (aromatic)	37.02	74.04
Group	2	-CN (to aromat)	59.89	119.78
*		Equation Constant		122.50

RESULT	MELTING POINT in deg Kelvin	348.84
	MELTING POINT in deg C	75.68

Water Sol from Kow (WSKOW v1 .41) Results:

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Water Sol: 1018 mg/L

SMILES : C(#N)c(cccclC(#N))cl

CHEM : 1,3-Benzenedicarbonitrile

MOL FOR: C8 H4 N2

MOL WT : 128.13

---------- WSKOW v1.41 Results ----------

Log Kow (estimated) : 1.09

Log Kow (experimental): 0.80

Cas No: 000626-I 7-5

Name : 1,3-Benzenedicarbonitrile

Refer : Hansch,C et al. (1995)

Log Kow used by Water solubility estimates: 0.80 (user entered)

Equation Used to Make Water Sol estimate:

Log S (mol/L) = 0.693-0.96 log Kow-0.0092(Tm-25)-0.00314 MW + Correction

Melting Pt (Tm) = 162.00 deg C (Use Tm = 25 for all liquids)

Correction(s):	Value
Nitrile	-0.362

Log Water Solubility (in moles/L) : -2.100

Water Solubility at 25 deg C (mg/L): 1018

WATERNT Program (v1 .01) Results:

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Water Sol (v1.01 est): 191.69 mg/L

SMILES : C(#N)c(cccclC(#N))cl

CHEM : 1,3-Benzenedicarbonitrile

MOL FOR: C8 H4 N2

MOL WT : 128.13

TYPE	NUM	WATER SOLUBILITY FRAGMENT DESCRIPTION	COEFF	VALUE
Frag	4	Aromatic Carbon (C-H type)	-0.3359	-1.3435
Frag	2	-CδN [cyano, aromatic attach]	-O.3255	-0.6509
Frag	2	Aromatic Carbon (C-substituent type)	-0.5400	-1.0799
Const		Equation Constant		0.2492

Log Water Sol (moles/L) at 25 dec C = -2.8251

Water Solubility (mg/L) at 25 dec C = 191.69

ECOSAR Program (v0.99g) Results:

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SMILES : C(#N)c(cccclC(#N))cl

CHEM : 1,3-Benzenedicarbonitrile

CAS Num:

ChemID1:

ChemID2:

ChemID3:

MOL FOR: C8 H4 N2

MOL WT : 128.13

Log Kow: 0.80 (User entered)

Melt Pt: 162.00 deg C

Wat Sol: 1.05E+004 mg/L (measured)

ECOSAR v0.99g Class(es) Found

Neutral Organics

ECOSAR Class	Organism	Duration	End Pt	Predicted mg/L (ppm)
Neutral Organic SAR (Baseline Toxicity)	: Fish	14-day	LC50	1909.260
Neutral Organics	: Fish	96-hr	LC50	1275.455
Neutral Organics	: Fish	14-day	LC50	1909.260
Neutral Organics	: Daphnid	48-hr	LC50	1257.955
Neutral Organics	: Green Algae	96-hr	EC50	733.948
Neutral Organics	: Fish	30-day	ChV	135.414
Neutral Organics	: Daphnid	16-day	EC50	38.165
Neutral Organics	: Green Algae	96-hr	ChV	36.683
Neutral Organics	: Fish (SW)	96-hr	LC50	163.555
Neutral Organics	: Mysid Shrimp	96-hr	LC50	866.294

dry wt soil

Neutral Organics : Earthworm 14-day LC50 1846.142

Note: * = asterick designates: Chemical may not be soluble enough to measure this predicted effect.

Fish and daphnid acute toxicity log Kow cutoff: 5.0

Green algal EC50 toxicity log Kow cutoff: 6.4

Chronic toxicity log Kow cutoff: 8.0

MW cutoff: 1000

HENRY (v3.10) Program Results:

Bond Est : 5.03E-007 atm-m3/mole

Group Est: 3.70E-007 atm-m3/mole

SMILES : C(#N)c(ccccIC(#N))cl

CHEM : 1,3-Benzenedicarbonitrile

MOL FOR: C8 H4 N2

MOL WT : 128.13

HENRYWIN v3.10 Results

CLASS	BOND CONTRIBUTION DESCRIPTION	COMMENT	VALUE
HYDROGEN	4 Hydrogen to Carbon (aromatic) Bonds		I-O.6172
FRAGMENT	6 Car-Car		1.5828
FRAGMENT	2 Car-CN		3.7213
RESULT	BOND ESTIMATION METHOD for LWAPC VALUE	TOTAL	4.687

HENRYs LAW CONSTANT at 25 deg C = 5.03E-007 atm-m3/mole

= 2.06E-005 unitless

GROUP CONTRIBUTION DESCRIPTION	COMMENT	VALUE
2 Car (CN)(Car)(Car)	ESTIMATE	4.38
4 Car-H (Car)(Car)		0.44
RESULT | GROUP ESTIMATION METHOD for LOG GAMMA VALUE |	TOTAL	4.82

HENRYs LAW CONSTANT at 25 deg C = 3.70E-007 atm-m3/mole

= 1.51 E-005 unitless

Henrys LC [VP/WSol estimate using EPI values]:

HLC: 9.136E-008 atm-m3/mole

VP: 0.00569 mm Hg

WS: 1.05E+004 mg/L

BIOWIN (v4.01) Program Results:

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SMILES : C(#N)c(ccccIC(#N))cl

CHEM : 1,3-Benzenedicarbonitrile

MOL FOR: C8 H4 N2

MOL WT : 128.13

---------- BIOWIN v4.01 Results ----------

Linear Model Prediction : Biodegrades Fast

Non-Linear Model Prediction: Biodegrades Fast

Ultimate Biodegradation Timeframe: Weeks

Primary Biodegradation Timeframe: Days-Weeks

MITI Linear Model Prediction : Biodegrades Fast

MITI Non-Linear Model Prediction: Does Not Biodegrade Fast

TYPE	NUM	BIOWIN FRAGMENT DESCRIPTION	COEFF	VALUE
Frag	2	Cyanide / Nitriles [-C#N]	0.3070	0.6140
MolWt	*	Molecular Weight Parameter		-0.0610
Const	*	Equation Constant		0.7475
RESULT		LINEAR BIODEGRADATION PROBABILITY		1.3005

TYPE	NUM	BIOWIN FRAGMENT DESCRIPTION	COEFF	VALUE
Frag	2	Cyanide / Nitriles [-C#N]	4.6440	9.2880
MolWt	*	Molecular Weight Parameter		I-1.8195
RESULT		NON-LINEAR BIODEGRADATION PROBABILITY		1.0000

A Probability Greater Than or Equal to 0.5 indicates --> Biodegrades Fast

A Probability Less Than 0.5 indicates --> Does NOT Biodegrade Fast

TYPE	NUM	BIOWIN FRAGMENT DESCRIPTION	COEFF	VALUE
Frag	2	Cyanide / Nitriles [-C#N]	I-O.0824	I-O.1648

MolWt| * | Molecular Weight Parameter | | -0.2832

Const| * | Equation Constant | | 3.1992

RESULT	SURVEY MODEL - ULTIMATE BIODEGRADATION		2.7513

TYPE	NUM	BIOWIN FRAGMENT DESCRIPTION	COEFF	VALUE
Frag	2	Cyanide / Nitriles [-C#N]	-0.0652	-0.1304
MolWt	*	Molecular Weight Parameter		-0.1849
Const	*	Equation Constant		3.8477

RESULT	SURVEY MODEL - PRIMARY BIODEGRADATION	3.5325

Result Classification: 5.00 -> hours 4.00 -> days 3.00 -> weeks

(Primary & Ultimate) 2.00 -> months 1.00 -> longer

TYPE	NUM	BIOWIN FRAGMENT DESCRIPTION	COEFF	VALUE
Frag	2	Cyanide / Nitriles [-C#N]	0.0717	0.1433
Frag	4	Aromatic-H	0.0082	0.0329
MolWt	*	Molecular Weight Parameter		I-O.3812
Const	*	Equation Constant		0.7121

RESULT	MITI LINEAR BIODEGRADATION PROBABILITY		0.5071

TYPE	NUM	BIOWIN FRAGMENT DESCRIPTION	COEFF	VALUE

Frag	2	Cyanide / Nitriles [-C#N]	0.2340	0.4679
Frag	4	Aromatic-H	0.1201	0.4806
MolWt	*	Molecular Weight Parameter		-3.6991
RESULT		MITI NON-LINEAR BIODEGRADATION PROBABILITY		0.4440

A Probability Greater Than or Equal to 0.5 indicates --> Readily Degradable

A Probability Less Than 0.5 indicates --> NOT Readily Degradable

AOP Program (v1 .91) Results:

SMILES : C(#N)c(cccc1 C(#N))c1

CHEM : 1,3-Benzenedicarbonitrile

MOL FOR: C8 H4 N2

MOL WT : 128.13

SUMMARY (AOP v1 .91): HYDROXYL RADICALS

Hydrogen Abstraction = 0.0000 E-12 cm3/molecule-sec

Reaction with N, S and -OH = 0.0000 E-12 cm3/molecule-sec

Addition to Triple Bonds = 0.0000 E-12 cm3/molecule-sec

Addition to Olefinic Bonds = 0.0000 E-12 cm3/molecule-sec

Addition to Aromatic Rings = 0.0608 E-12 cm3/molecule-sec

Addition to Fused Rings = 0.0000 E-12 cm3/molecule-sec

OVERALL OH Rate Constant = 0.0608 E-12 cm3/molecule-sec

HALF-LIFE = 175.947 Days (12-hr day; 1.5E6 OH/cm3)

(AOPv1.91):OZONEREACTION

****** NO OZONE REACTION ESTIMATION ******

(ONLY Olefins and Acetylenes are Estimated)

Experimental Database: NO Structure Matches

PCKOC Program (v1 .66) Results:

Koc (estimated): 307

SMILES : C(#N)c(cccc1 C(#N))c1

CHEM : 1,3-Benzenedicarbonitrile

MOL FOR: C8 H4 N2

MOL WT : 128.13

PCKOCWIN v1.66 Results

First Order Molecular Connectivity Index ..... : 4.864

Non-Corrected Log Koc ..... : 3.2096

Fragment Correction(s):

* Nitrile/Cyanide (-CδN) ..... : -0.7223

Corrected Log Koc ..... : 2.4873

Estimated Koc: 307.1

HYDROWIN Program (v1 .67) Results:

SMILES : C(#N)c(cccc1C(#N))c1

CHEM : 1,3-Benzenedicarbonitrile

MOL FOR: C8 H4 N2

MOL WT : 128.13

---------- HYDROWIN v1 ----------

Currently, this program can NOT estimate a hydrolysis rate constant for the type of chemical structure entered!!

ONLY Esters, Carbamates, Epoxides, Halomethanes (containing l-3 halogens) and Specific Alkyl Halides can be estimated!! For more information, (Click OVERVIEW in Help or see the User's Guide)

***** CALCULATION NOT PERFORMED *****

BCF Program (v2.15) Results:

SMILES : C(#N)c(cccclC(#N))cl

CHEM : 1,3-Benzenedicarbonitrile

MOL FOR: C8 H4 N2

MOL WT : 128.13

---------- Bcfwin v2.15 ----------

Log Kow (estimated) : 1.09

Log Kow (experimental): 0.80

Log Kow used by BCF estimates: 0.80 (user entered)

Equation Used to Make BCF estimate:

Log BCF = 0.50

Correction(s): Value

Correction Factors Not Used for Log Kow < 1

Estimated Log BCF = 0.500 (BCF = 3.162)

Volatization From Water

Chemical Name: 1,3-Benzenedicarbonitrile

Molecular Weight : 128.13 g/mole

Water Solubility : 1.05E+004 ppm

Vapor Pressure : 0.00569 mm Hg

Henry's Law Constant: 5.03E-007 atm-m3/mole (entered by user)

	RIVER	LAKE
Water Depth (meters):	1	1
Wind Velocity (m/sec):	5	0.5
Current Velocity (m/sec):	1	0.05

HALF-LIFE (hours) :	1319	1.448E+004
HALF-LIFE (days) :	54.95	603.4
HALF-LIFE (years) :	0.1504	1.652

STP Fugacity Model: Predicted Fate in a Wastewater Treatment Facility

PROPERTIES OF: 1,3-Benzenedicarbonitrile

Molecular weight (g/mol)	128.13
Aqueous solubility (mg/l)	10500
Vapour pressure (Pa)	0.758604
(atm)	7.48684E-006
(mm Hg)	0.00569
Henry's law constant (Atm-m3/mol)	5.03E-007
Air-water partition coefficient	2.05712E-005
Octanol-water partition coefficient (Kow)	6.30957
Log Kow	0.8
Biomass to water partition coefficient	2.06191
Temperature [deg C]	25

Biodeg rate constants (h^-1),half life in biomass (h) and in 2000 mg/L MLSS (h):

-Primary tank	0.02	41.07	10000.00
-Aeration tank	0.02	41.07	10000.00
-Settling tank	0.02	41.07	10000.00

STP Overall Chemical Mass Balance:

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	g/h	mol/h	percent
Influent	1.00E+001	7.8E-002	100.00
Primary sludge	2.65E-002	2.1 E-004	0.26
Waste sludge	1.51E-001	1.2E-003	1.51
Primary volatilization	2.74E-004	2.1 E-006	0.00
Settling volatilization	7.45E-004	5.8E-006	0.01
Aeration off gas	1.84E-003	1.4E-005	0.02
Primary biodegradation	1.76E-003	1.4E-005	0.02
Settling biodegradation	5.28E-004	4.1E-006	0.01
Aeration biodegradation	6.95E-003	5.4E-005	0.07

Final water effluent	9.81 E+000	7.7E-002	98.10
Total removal	1.90E-001	1.5E-003	1.90
Total biodegradation	9.24E-003	7.2E-005	0.09

Level III Fugacity Model (Full-Output):

==========

Chem Name : 1,3-Benzenedicarbonitrile

Molecular Wt: 128.13

Henry's LC : 5.03e-007 atm-m3/mole (user-entered)

Vapor Press : 0.00569 mm Hg (user-entered)

Liquid VP : 0.129 mm Hg (super-cooled)

Melting Pt : 162 deg C (user-entered)

Log Kow : 0.8 (user-entered)

Soil Koc : 2.59 (calc by model)

	Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)
Air	6.52	4.22e+003	1000
Water	46.5	360	1000
Soil	46.9	360	1000
Sediment	0.0817	1.44e+003	0

	Fugacity (atm)	Reaction (kg/hr)	Advection (kg/hr)	Reaction (percent)	Advection (percent)
Air	1.27e-010	1 1	669	0.366	22.3
Water	9.36e-012	918	477	30.6	15.9
Soil	2.9e-010	925	0	30.8	0
Sediment	7.74e-012	0.403	0.0168	0.0134	0.000559

Persistence Time: 342 hr

Reaction Time: 553 hr

Advection Time: 895 hr

Percent Reacted: 61.8

Percent Advected: 38.2

Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):

Air: 4222

Water: 360

Soil: 360

Sediment: 1440

Biowin estimate: 2.751 (weeks)

Advection Times (hr):

Air: 100

Water: 1000

Sediment: 5e+004

Appendix 2: Information on the negative and positive control substances used in the isophthalonitrile Ames assay.

CTL Report Number: CTL/C/3277 Salmonella/Mammalian-Microsome Plate Incorporation Assay (Ames Test) With And Without Renal Activation With Isophthalonitrile (IPN)

Sponsor: SDS Biotech Corp, Agricultural Chemicals Business, Painesville, Ohio 44077 Testing Facility: Microbiological Associates, Inc., Bethesda MD, USA
Authors: Jones R and Killeen J (1985)

Information on the negative and positive control substances:

METHOD:

Positive controls: 2-Aminoanthracene (used with activation for all strains)
2-Nitrofluorene (used without activation for TA98 and TA1 538)
Sodium azide (used without activation for TA1 00 and TA1 535)
9-Aminoacridine (used without activation for TA1 537)

All combinations of positive controls and tester strains plated along with the assay are listed below:

Strain	Activation	Positive controls	Conc. per plate µg
TA98	+	2-Aminoanthracene	4.0
TA98		2-Nitrofluorene	5.0
TA100	+	2-Aminoanthracene	4.0
TA100		Sodium azide	5.0
TA1535	+	2-Aminoanthracene	4.0
TA1535		Sodium azide	5.0
TA1537	+	2-Aminoanthracene	4.0
TA1537		9-Aminoacridine	75.0
TA1538	+	2-Aminoanthracene	4.0
TA1538		2-Nitrofluorene	5.0

Solvent controls: Ethanol (95%) or acetone solvent control was plated for all strains with and without metabolic activation.

The following criteria had to be met for the assay to be considered valid:

a) Solvent control values must be within acceptable limits as determined by the laboratory.

b) Positive control values must exhibit at least a three-fold increase in the number of revertants per plate over an average value for the solvent control for the respective strain.

RESULTS

Positive control data for Experiment No. T2580-B1 (plated 12 November 1984)

Strain	Chemical	Conc per plate µg	Metabolic activation	Revertants/plate			Averaged revertants /plate	S.D.
TA98	2-Aminoanthracene	4.0	Rat kidney*	27	24	35	29	6
TA98	2-Nitrofluorene	5.0	None	980	826	817	874	92
TA100	2-Aminoanthracene	4.0	Rat kidney*	99	98	105	101	4
TA100	Sodium Azide	5.0	None	1241	1427	1184	1284	127
TA1535	2-Aminoanthracene	4.0	Rat kidney*	12	20	11	14	5
TA1535	Sodium Azide	5.0	None	1036	1079	916	1010	84
TA1537	2-Aminoanthracene	4.0	Rat kidney*	8	7	7	7	1
TA1537	9-Aminoacridine	75	none	522	574	363	486	110
TA1538	2-Aminoanthracene	4.0	Rat kidney*	36	45	21	34	12
TA1538	2-Nitrofluorene	5.0	none	1480	1349	1507	1445	85

[Colonies were machine counted.]

* In Experiment T2580-B1, the positive control values for the tester strains in the presence of metabolic activation did not meet the requirements specified in the protocol (the cause of the invalid positive control values with activation was identified as a plating procedural problem with the positive controls rather than a problem with the test system). The portion of the assay with metabolic activation was retested in Experiment T2580-B2.

Solvent Control for T2580-B1 – Acetone 100µl

Strain	Cells seeded $x10^8$	Kidney microsomes	Revertants/plate			Averaged revertants	S.D.
TA98	0.9	Rat*	13	22	23	19	6
TA98	0.9	None	14	15	16	15	1
TA100	1.2	Rat*	82	114	86	94	17
TA100	1.2	None	81	82	87	83	3
TA1535	1.0	Rat*	6	5	6	6	1
TA1535	1.0	None	8	11	7	9	2
TA1537	0.8	Rat*	3	5	6	5	2
TA1537	0.8	None	4	6	2	4	2
TA1538	1.0	Rat*	14	9	10	11	3
TA1538	1.0	None	11	11	6	9	3

* [Colonies were hand counted.]

Positive control data for Experiment No. T2580-B2 (plated 19 November 1984)

Strain	Chemical	Conc per plate µg	Metabolic activation	Revertants/plate			Averaged revertants/ plate	S.D.
TA98	2-Aminoanthracene	4.0	Rat kidney	3301	3347	3415	3354	57
TA98	2-Nitrofluorene	5.0	None	967	878	936	927	45
TA100	2-Aminoanthracene	4.0	Rat kidney	3284	3622	3492	3466	170
TA100	Sodium Azide	5.0	None	1893	1622	1470	1662	214
TA1535	2-Aminoanthracene	4.0	Rat kidney	284	279	282	282	3
TA1535	Sodium Azide	5.0	None	1561	1662	1522	1582	72

[Colonies were machine counted.]

$ In Experiment T2580-B2, tester strain TA1537 had an invalid strain characterisation. Thus, test strain TA1537 was retested in Experiment T2580-B3

Solvent Control for T2580-B2 – Acetone 100µl

Strain	Cells seeded $x10^8$	Kidney microsomes	Revertants/plate			Averaged revertants	S.D.
TA98	1.2	Rat	31	23	27	27	4
TA100	0.9	Rat	94	124	97	105	17
TA1535	1.2	Rat	9	12	7	9	3

[Colonies were hand counted.]

Positive control data for Experiment No. T2580-B3 (plated 3 December 1984)

Strain	Chemical	Conc per plate µg	Metabolic activation	Revertants/plate			Averaged revertants/ plate	S.D.
TA1537	2-Aminoanthracene	4.0	Rat kidney	410	450	556	472	75
TA1537	9-Aminoacridine	75	None	547	310	532	463	133
TA1538	2-Aminoanthracene	5.0	Rat kidney	2386	2561	3031	2659	334
TA1538	2-Nitrofluorene	counted.]	None	1790	1727	1796	1771	38

[Colonies were machine

Solvent Control for T2580-B3– Acetone 100µl

Strain	Cells seeded $xl\ 0^8$	Kidney microsomes	Revertants/plate			Averaged revertants	S.D.
TA1537	0.9	Rat	15	14	11	13	2
TA1537	0.9	None	5	7	7	6	1
TA1538	0.9	Rat	15	23	30	23	8

[Colonies were hand counted.]